b.) Remarks

Claims 16 and 42 have been amended in order to recite the present invention with the specificity required by statute. Additionally, claims 19, 20, 35, 43 and 44 are amended for better conformity with their antecedent claims. The subject matter of the amendment may be found in the specification as filed, *inter alia*, at page 7, lines 20-26, page 13, lines 15-16 and page 14, line 4, etc. Accordingly, no new matter has been added.

Claims 16, 19-20, 23, 25, 35, 37, 39, 42-44 and 46-48 are rejected under 35 U.S.C. §102 (b) as anticipated by either Woodle (U.S. Patent No. 5,356,633) or Woodle (U.S. Patent No. 5,014,556). The Examiner states that the arguments presented in Applicants' July 7, 2004 Amendment are incorrect, pointing to example 4 of Woodle '633 and examples 4 and 7 of Woodle '556. Woodle '633 example 4 provides liposomes, averaging 0.17 and 0.16 micron diameter, of hydrogenated soy phosphatidylcholine or PEG-DSPE containing NSAID or methotrexate. Woodle '556 is cumulative.

This rejection is respectfully traversed in view of the foregoing amendment. In particular, neither Woodle patent teaches or suggests the pharmaceutical composition or the liposome preparation recited in amended claims 16 and 42, which encapsulate an indolocarbazole derivative.

Claims 16, 23-25, 35, 37-39, 42 and 46-48 are also rejected as anticipated by Allen (U.S. Patent No. 4,920,016). Similarly to Woodle '633 and '556, Allen is relied on as disclosing liposomes made from DSPC having a diameter of 170 nm and containing anti-tumor agents or antibiotics. However, Allen too does not teach or suggest liposomes which encapsulate an indolocarbazole derivative.

Claims 16, 19-20, 22-23, 25, 35-39, 42-46 and 48 are rejected under 35 U.S.C. §103 as being obvious Kato (EP 0 850,646) in optional view of Woodle '633. Kato discloses liposome formulations containing indolocarbazole derivatives. The liposomes are made from hydrogenated phospholipids and PEG-DSPE.

In this regard, the Examiner acknowledges that Kato does not explicitly state that the sizes of the liposomes but notes that, absent a showing of criticality, it would have been obvious to one of ordinary skill in the art to prepare liposomes of desired size with the expectation of obtaining the best possible results. Woodle is relied upon for showing preparing liposomes of different sizes is routine in this art.

In response, Applicants wish to point out the criticality of average particle size for liposomes containing indolocarbazoles. In this regard, Kato Test Example 2 (see page 7, lines 21-44) shows that liposomes of phosphatidylcholine containing UCN-01[1/] are reasonably stable in buffer over time.

However, Applicants have determined that stability of liposomes in buffer is not a good model for stability in the presence of a biological component, e.g., in blood. This is confirmed because liposomes made from phosphatidylcholine (all examples of Kato EP '646 and Comparative Example 2 of the present invention) showed inhibited leakage in buffer solution but not inhibited leakage in rat plasma (see Test Example 1 from page 13, line 23 to page 16, line 18 of in the present invention).

As seen in Applicants' Table 1 at specification page 16, hydrogenated soybean phosphatidylcholine liposomes having an average particle size of 109 nm

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1/ An indolocarbazole derivative

(comparative example 1) lost 59% of UCN-01 after 3 hours. The same liposomes having an average particle size of 186 or 130 nm (examples 1 and 2) lost only 16 and 37% of UCN-01 after 3 hours, respectively.

This remarkable advantage --an average improvement of 55%-- is plainly useful to those of ordinary skill in this art, and is entirely unobvious in view of the prior art.

Therefore, those of ordinary skill in the art would not expect, from the inhibition of leakage in the absence of a biological component as described in Kato, that liposomes satisfying both the lipid and the size of the present invention can significantly inhibit leakage of indolocarbazole derivative in the presence of a biological component.

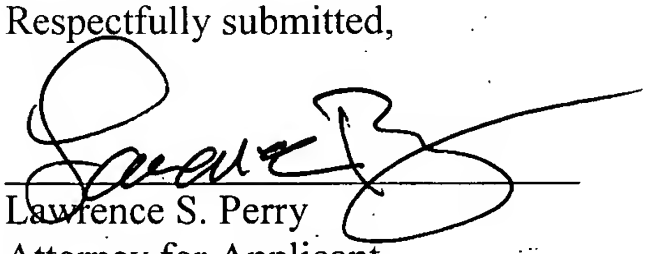
The last remaining issue, therefore, is the rejection of claims 24 and 38 as being obvious over Woodle '633 or '556 by themselves or in view of Mauer, *BBA*, 1998, 1374, pp. 9-20, of record, and of claims 22 and 36 as being obvious over Woodle '633 or '556 in combination with Kato EP '646. In response, solely in order to reduce the issues, these claims have been cancelled. Nonetheless, as to the amended claims, Applicants wish to explain that neither Woodle '633 or '556 suggest the remarkable inhibition of leakage of indolocarbazole derivatives in the presence of a biological component that is attained by the present invention.

In view of the above amendments and remarks, Applicants submit that all of the Examiner's concerns are now overcome and the claims are now in allowable condition. Accordingly, reconsideration and allowance of this application is earnestly solicited.

Claims 16, 19, 20, 35 and 42-44 remain presented for continued prosecution.

Applicant's undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,



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